Abstract
The equivalence of the US Orange Book in China, the “CN Orange Book” has been operating since 29 June 2021. This “CN Orange Book” is a mountain full of treasures, for example clear indication on what claim is covering which subject matter in a particular drug patent. This “unofficial” user guide aims to provide foreigners information on how to navigate this “CN Orange Book”, which operates in Chinese.
In the US, the Orange Book is a publication from the US FDA that identifies drug products with marketing approval from the FDA and related patent and exclusivity information. Information in the Orange Book could be used in actions under the Hatch-Waxman Act, which allows a patentee to file an artificial act of infringement that allows the drug innovator to file suit before the generic drug is commercialized, such that the drug marketing approval process of the generic drug at the US FDA could be suspended.

China is required to introduce a similar system under the Phase-I trade agreements signed with the US in January 2020. I have been following this since then, and have several articles and posts on this topic. Recently, this “CN Orange Book” (official name: China listed drugs patent information registration platform) has become officially online on 29 June 2021, with many developments thereafter, and I have received many questions on how to use this. This motivates me to write this “unofficial” user guide, mainly for foreign users. This user guide may need updates periodically as things are changing too fast in China.

The equivalence of the US FDA in China is the China National Medical Products Administration, the NMPA.

This is the October 2021 version of this guide, as there have been many developments shortly after my first July version was finished on 19 July 2021.
Available to anyone, but could only search in Chinese

The “CN Orange Book” is available at https://zldj.cde.org.cn/home. Anyone can access information therein. Below is a screen shot of the first page showing different functions thereon:
For searching drug patent information already registered, the information is divided into three tabs, each respectively directed to Chinese medicine, chemical drug, and biological drugs as shown below (with the tab of chemical drugs chosen):

![Search interface for drug patent information](image)

Searches could be done and directed to the drug name, the format of the drug, dosage, and the drug marketing number at the NMPA. Mostly the name of the drug is used. Partial search for drug patent information already registered is available, but could only be done in Chinese. For example, using only the last three words of Palbociclib in Chinese (“柏西利” in "哌柏西利") resulted in the following search results:
**Extensive information contained therein – good for FTO research**

The “CN Orange Book” has the following number of entries as of different dates in the table below:

<table>
<thead>
<tr>
<th>Type of drugs</th>
<th>30 June 2021 no.</th>
<th>19 July 2021 no.</th>
<th>3 October 2021 no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese medicines</td>
<td>30</td>
<td>143</td>
<td>243</td>
</tr>
<tr>
<td>Chemical drugs</td>
<td>278</td>
<td>448</td>
<td>532</td>
</tr>
<tr>
<td>Biological drugs</td>
<td>39</td>
<td>60</td>
<td>78</td>
</tr>
</tbody>
</table>

There was a relatively big surge in July 2021, shortly after the database was firstly introduced on 29 June 2021, while the number of registrations slowed down significantly thereafter. This could be expected, as every drug owner would rush into the register at the beginning.
One amazing feature of the “CN Orange Book” is the inclusion of extensive data in each entry. Below is a screenshot of the entry in the “CN Orange Book” for the drug Palbociclib capsule 125mg (Note: only part of the entries of one of the three patents registered for this drug is shown below due to limit of the screen shot that could be taken):

It can be seen that in addition to the patent number, the following information in the “CN Orange Book” database entries is also available:

1) The granted patent itself is available for downloading at a link on the same page.
2) The claim number(s), and the relevant subject matter, are clearly identified.
3) The full-term expiry of the patent(s) is clearly identified.
4) Whether the patent has survived through invalidation is also specified in the note section.
On the other hand, there exists entries without the above extensive information of 1)-4), as shown below as of 19 July 2021:

<table>
<thead>
<tr>
<th>相关专利号</th>
<th>专利名称</th>
<th>专利申请人</th>
<th>专利权人</th>
<th>专利权人地址</th>
<th>专利权人联系方式</th>
<th>专利权人邮箱</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZL03821144.0</td>
<td>包含新型农药的三元组合物</td>
<td>莱比锡的产权有限责任公司</td>
<td>莱比锡的产权有限责任公司</td>
<td>莱比锡的产权有限责任公司</td>
<td>莱比锡的产权有限责任公司</td>
<td>莱比锡的产权有限责任公司</td>
</tr>
</tbody>
</table>

专利权人：莱比锡的产权有限责任公司  
专利权人地址：莱比锡的产权有限责任公司  
专利权人联系方式：莱比锡的产权有限责任公司  
专利权人邮箱：莱比锡的产权有限责任公司  

**授权证明文件：**  
文件1：优先权证书-ZL03821144.0-专利证书.pdf  
文件2：优先权证书-ZL03821144.0-法律状态.pdf  
文件3：优先权证书-ZL03821144.0-授权证书.pdf

**上市许可持有人与专利权人关系：**  
上市许可持有人与专利权人无直接关系  
上市许可持有人与专利权人无间接关系  

**药物相关专利权利要求：**  
<table>
<thead>
<tr>
<th>序号</th>
<th>权利要求编号</th>
<th>专利类型</th>
<th>专利权保护期</th>
<th>状态</th>
<th>备注</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

上市许可持有人联系方式：
- 姓名：刘红霞  
- 联系电话：010-65693290
The same entry above has its information updated as of 3 October 2021, indicating claims 5 to 8 of the relevant patent CN ZL03821144.0 are directed to the drug composition containing the active pharmaceutical ingredient API vardenafil hydrochloride trihydrate:

<table>
<thead>
<tr>
<th>相关专利号</th>
<th>相关专利类型</th>
<th>专利号</th>
<th>专利保护期届满日</th>
<th>状态</th>
<th>备注</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZL03821144.0</td>
<td>化学药品组合物的药物组合物专利</td>
<td>2023-07-03</td>
<td>有效</td>
<td></td>
<td>Updated patent claim information</td>
</tr>
</tbody>
</table>

It should be noted that the relevant regulations, the NMPA Measures (see below) put the onus on the patentee/drug marketing approval holder DMAH to ensure the accuracy of the information registered on the platform, which requires the claim(s) covering what aspect of the drug to be identified (Article 4 of the NMPA Measures). Failure to do so could be legally liable (Article 15 of the NMPA Measures), while it is unclear exactly what the punishments are.

Most of the entries in the “CN Orange Book” contain extensive information like the one of Palbociclib capsule 125mg above (if not, updated could be expected). Such information could be very useful for a freedom-to-operate (FTO) exercise. The immediate availabilities of the grant patent publication and the full-term expiry are already very useful. The specific identifications of the claim(s) and relevant subject matter are even more so.
By contrast, the equivalent FDA records only contain the US patent numbers and the full term expiry date, but nothing further. Below is the screenshot of Palbociclib capsule 125mg in the US FDA Orange Book records:

**Patent and Exclusivity for: N207103**

Restrictions on the type of patents that could be registered

The “CN Orange Book” restricts that only the following types of patents could be registered for the respective drugs (Articles 5 and 12 of the NMPA Measures):

- Chemical drugs – chemical compound of the active ingredient; composition comprising the active ingredient; medical use
- Biological drug – sequence structure of the active ingredient; medical use
- Chinese medicine – composition; extracts from Chinese medicine; medical use

While not specified in the articles of the NMPA measures, the accompanying explanations of the NMPA measures specify that patents covering intermediates, metabolites, crystal form, method of manufacturing and testing methods are not considered as relevant patents under the patent linkage system, i.e. these patents should not be registered on the “CN Orange Book”. Therefore, the above types of patents would not be seen in the “CN Orange Book”.

Having said so, one way to get around the restriction on crystal form is to record a patent having a composition claim, or medical use claims (in the form of Swiss-type claim, as method of treatment is not patentable in China) containing the crystal form of the API. An example will be shown below in the first contentious drug patent linkage declaration.
Only Chinese company could register, and make entries on the platform

While everyone could access the platform to view information therein, in order to register entries on the platform (either for a drug, or making a declaration against a drug), one must register as a user on the platform. However, only a Chinese company could do so, as it is required to input the so-called "unified social credit codes" (compulsory) during registration, which are available to all Chinese companies. Further, the registration requires a CN mobile number to complete (for receiving a confirmatory text message).

See the screenshot below:

Declaration from a generic drug applicant against an innovative drug

For details on how such a declaration works, please refer to my articles below:

https://www.linkedin.com/pulse/cn-patent-inkage-measures-trial-finalized-issued-nmpa-toby-mak (This article talks about the finalized NMPA measures, which is based on the draft measures below)

https://www.linkedin.com/pulse/cn-drug-patent-registration-system-orange-book-opened-toby-mak (This article talks about the draft NMPA measures)
As a summary, when a generic drug applicant applies for drug marketing approval at the NMPA, the generic drug applicant is required to make a declaration of any one of the following four types:

I) That there is no patent information registered related to the drug.

II) That the patent(s) has already expired, or been declared invalid.

III) The date on which the patent(s) will expire, and that generic applicant promises that the generic drug will not go on the market until the expiry of the patent(s).

IV) That the patent(s) is not infringed, or should be declared invalid.

As of 3 October 2021, 410 declarations have been announced on the CN platform, with vast majority being type I) to III) declarations. The first type III) declaration was announced on 9 July 2021, with the screenshot below:

The key is the type of declaration filed, in the screenshot above being type III). It should also be noted that this page subdivides Declaration type IV) into the following two types:

- 4.1 - The patent(s) should be declared invalid.
- 4.2 – The generic drug does not fall within the scope of the patent(s).
The type of the declaration determines whether the drug patentee/DMAH could take action against the subject generic drug marketing approval application. It appears only action could be taken against declaration type 4.2 (the generic drug does not fall within the scope of the patent(s)). While Article 7 of the NMPA measures could be literally read as allowing complaints to be filed at a court or the CNIPA for all 4 types of declarations, when combining with the relevant measures of the Supreme People’s Court and the CNIPA, it appears that there is a typographical error in Article 7 of the NMPA measures, and complaint could only be filed for declaration type 4.2.

Type 4.1 declaration has already been announced, with an example shown below:

<table>
<thead>
<tr>
<th>序号</th>
<th>通用名中英文</th>
<th>专利号</th>
<th>专利类型</th>
<th>持有人名称</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ticagrelor 90mg tablet</td>
<td>AstraZeneca AB</td>
<td>4.1类</td>
<td>AstraZeneca</td>
</tr>
</tbody>
</table>

In the above, the drug at issue is ticagrelor 90mg tablet, with AstraZeneca being the DMAH, and the generic drug applicant being Shanxi Deyuantang Pharmaceutical Co., Ltd. (Deyuantang). In this situation, there is nothing AstraZeneca could do to delay the drug marketing approval process of the generic ticagrelor 90mg tablet from Deyuantang at the NMPA.

**The first type 4.2 declaration**

This was announced on 23 July 2021 directed to the drug dapagliflozin (达格列净) 5 and 10 mg, with AstraZeneca as the DMAH in China. The relevant screen shot for the 5mg drug is shown below, while that of the 10 mg drug has similar contents.
It is interesting to note that the generic drug applicant Jiangsu Hansoh Pharmaceutical Group Co., Ltd. (江苏豪森药业集团有限公司, Hansoh) filed a type III) declaration against CN200910158686.6 directed to the chemical compound of the API dapagliflozin itself, i.e. Hansoh undertakes that they would only put their drug onto the market after CN200910158686.6 has expired on 15 May 2023 (CN200910158686.6 is a divisional from CN03811353.8).

On the other hand, Hansoh filed type 4.2 declarations against the following 3 CN patents, i.e. Hansoh declared that their generic drug does not fall within the scope of the following 3 CN patents that are directed to specific formulations and medical uses:

1) CN200880016902.7 (full term expiry 21 March 2028) - specific formulation comprising the API in the form of dapagliflozin propylene glycol hydrate, microcrystalline cellulose, lactose, crospovidone, silicon dioxide, magnesium stearate, with each components presents in respective specific amounts (claim 8).

2) CN200780024135.X (full term expiry 21 June 2027) - Medical use (Swiss-type claim) of dapagliflozin propylene glycol hydrate with specific crystalline structure (note: as mentioned above patents directed to crystalline structure of a drug per se should not be registered in the CN Orange Book) in treating diabetes, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol,
hyperlipidemia, dyslipidemia, obesity, hypertriglyceridemia, or diabetic complications (claim 9).

3) CN201210201489.X (full term expiry 21 March 2028) - specific formulation comprising the API in the form of dapagliflozin propylene glycol hydrate with a specific dosage regime (claim 1), with further components including bulking agent, binder, disintegrant, and so on (claims 2 and 3), and the medical uses of such specific formulation (Swiss-type claims) for treating diabetes.

For 2), it should be noted that the patent is in fact directed to the crystal form of the API in the form of dapagliflozin propylene glycol hydrate, and therefore the CN Orange Book registration is directed to the medical use in Swiss-type claim containing such specific crystal form. Therefore, for China, it is important to include at least one composition or medical use Swiss-type claim for drug crystal form patent.

According to the above, Hansoh chose to challenge the patents directed to specific formulations comprising the API dapagliflozin propylene glycol hydrate, and the medical use of the crystalline API. Comparing with the chemical compound patent CN200910158686.6 (which Hanson chose to deal with using a type III declaration), there is higher chance to get around these formulation and medical use patents, for example by not using dapagliflozin propylene glycol hydrate, but uses dapagliflozin itself (whether this would be caught by equivalence is another question). In fact, Hanosh declared that the API in their generic drug is different from that in these 3 CN patents, i.e. dapagliflozin propylene glycol hydrate.

AstraZeneca had until 6 September 2021 (45 days from 23 July 2021) to file a complaint against Hansoh's type 4.2 declaration against the 3 CN patents above at the Beijing IP Court, or at the CNIPA. Failure to do so would result in that the drug marketing approval application would be processed as normal by the China National Medical Products Administration as usual, i.e. without any delay.

If AstraZeneca filed the complaint and was accepted (by the the Beijing IP Court, or the CNIPA), and a decision was made within 9 months from the date of acceptance of the complaint:
• if the decision was in favor of AstraZeneca, the drug marketing approval would be delayed to shortly before the expiry of the above three patents, i.e. maximum delay up to 2028.
• if the decision was not in favor of AstraZeneca or not within 9 months, the drug marketing approval would be processed as normal with no delay.

However, as Hanosh undertakes a type 3 declarations against CN200910158686.6, the earliest date that Hanosh could put their generic drug on the market in China is 15 May 2023.

I have tried to check whether AstraZeneca had filed the compliant at the Beijing IP Court the CNIPA by 6 September 2021, but no luck. In light of the relative ease of getting around the above three subject patents, and Hansoh undertakes that they would only put their drug onto the market after 15 May 2023, AstraZeneca may choose not to file the compliant against the type 4.2 declarations.

**Conclusion**

While the “CN Orange Book” is based on the US Orange Book (as required under the US-CN trade agreements 2021), the Chinese system has the following characteristics:

a) The patent information in the Chinese system is much more extensive than that of the US.
b) There is no drug data exclusivity information in the Chinese system.
c) Action could only be taken against type 4.2 declaration (the generic drug does not fall within the scope of the patent(s)) in China.

Regarding c), this may be the substantive difference of the CN system from the US system. In essence, in China, there is nothing the DMAH could do to delay the drug marketing approval process at the NMPA if the generic drug applicant simply alleges that the patent at issue should be declared invalid, and does not even challenge the validity of the patent afterwards.

There have been many changes on the “CN Orange Book” since its establishment on 29 June 2021. For example, in the very beginning, the platform does not have different tabs for entries of chemical drug, biological drug, and Chinese medicine. Now individual tabs
are available, making searching and counting much easier. Finally, all five types (types I to III), 4.1, and 4.1) declarations have been announced.

If you are an innovative drug owner, I am not surprised that you have already registered your drug patent information on the “CN Orange Book” to deter generic drug marketing approval application.

For others, including myself heavily involved in drug freedom-to-operate work, the “CN Orange Book” is a mountain full of treasures. Once the Chinese drug name is known (hint: have a look at the drug innovator’s Chinese website), the grant patent publication, claim(s) and subject matter(s) relevant (with clear indication on what claim is covering which subject matter), full term expiry, and invalidation information (if available) are all available in one place.

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